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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/757,616	01/13/2004	Rima Kaddurah-Daouk	MBZ-001CN	4792

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LAHIVE & COCKFIELD, LLP.
28 STATE STREET
BOSTON, MA 02109

EXAMINER	
CALAMITA, HEATHER	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 08/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/757,616	KADDURAH-DAOUK ET AL.	
	Examiner	Art Unit	
	Heather G. Calamita, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 May 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *73-84* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *73-84* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

5.00

DETAILED ACTION

Status of Application, Amendments, and/or Claims

1. Claims 73-84 are currently pending and under examination. Any objections and rejections not reiterated below are hereby withdrawn.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 73-84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Niebroj-Dobosz et al. (*Acta Neruol Scand*, July 1999) in view of Rashed et al. (Clinical Chemistry, 1997).

Niebroj-Dobosz et al. teach (claims 73-75) a method for identifying small molecules relevant to a nervous system disorder, comprising:

obtaining a small molecule profile of a subject suffering from a nervous system disorder (Glutamate, aspartate, glycine and GABA are amino acids which have the molecular weights of 147, 133, 75 and 105.13 Daltons, respectively, and therefore meet the claim limitation of small molecule which is defined in the specification as molecules with a molecular weight of less than 2000 Daltons (see p. 6 abstract); and

comparing the small molecule profile to a standard small molecule profile thereby, identifying the small molecules relevant to said nervous system disorder (see p. 6 abstract). Glutamate, aspartate, glycine and GABA fall into the category of electrochemically active or electrochemically neutral.

With regard to claims 76, 78 and 84 Niebroj-Dobosz et al. teach molecule profiles are obtained using HPLC (see p. 6 abstract).

With regard to claim 77, Neibroj-Dobosz et al. teach obtaining a small molecule profile of a subject suffering from a nervous system disorder (Glutamate, aspartate, glycine and GABA are amino acids which have the molecular weights of 147, 133, 75 and 105.13 Daltons, respectively, and therefore meet the claim limitation of small molecule which is defined in the specification as molecules with a molecular weight of less than 2000 Daltons (see p. 6 abstract);

identifying the small molecules relevant to said nervous system disorder using the small molecule profile, wherein the small molecule profile comprises information regarding the presence of two or more types of small molecules selected from the group consisting of sugars, fatty acids, amino acids, nucleotides, metabolites and products of catabolism (see p. 6 abstract). Glutamate, aspartate, glycine and GABA are amino acids, catabolites and metabolites.

With regard to clam 79, Niebroj-Dobosz et al. teach the nervous system disorder is a neurogenerative disorder (see p. 6 abstract).

With regard to claims 80 and 81, Niebroj-Dobosz et al. teach the nervous system disorder is Amyotrophic lateral sclerosis (see p. 6 abstract).

With regard to claim 82, Niebroj-Dobosz et al. teach the subject is human (see p. 7 col. 1 lines1 under patients).

With regard to claim 83, Niebroj-Dobosz et al. teach the small molecule profiles are obtained from the subjects blood, spinal fluid, serum, cells, tissue or cellular organelles (see p. 7 col. 1 lines1 under biochemical analysis).

Niebroj-Dobosz et al. do not teach (claims 73 and 74) detecting 50 or more or 50% or more of the small molecules in a sample.

Rashed et al. teach detecting 50 or more or 50% or more of the small molecules in a sample (see abstract and Figures 1 and 2).

One of ordinary at the time the invention was made would have been motivated to

apply the method of identifying small molecules relevant to ALS as taught by Niebroj-Dobosz et al. with the method of screening all the molecules in the blood with electrospray tandem mass spectrometry, as taught by Rashed et al. in order to have a specific and accurate high throughput method for screening for metabolic abnormalities. Rashed et al. state, " Metabolic profiling of free carnitine and acylcarnitine in plasma, blood spots or urine by various spectrophotometric, radiochemical or mass-spectrometic methods provides a powerful selective screening tool for these disorders (see p. 1130 col. 1 2nd sentence)." It would have been prima facie obvious to apply the method of identifying small molecules relevant to ALS as taught by Niebroj-Dobosz et al. with the method of screening all the molecules in the blood with electrospray tandem mass spectrometry, as taught by Rashed et al. in order to determine abnormalities in the molecules from blood spots, plasma, tissue or serum in people with ALS in a similar manner as Rashed with metabolic profiling of newborns for aminoacidopathies.

Response to Arguments

3. Claims 56-58 and 60-62 rejected under 35 U.S.C. 102(b) as being anticipated by Siman (USPN 5,871,712, 02/16/1999) have been withdrawn in view of the amendment.

Applicants' arguments with respect to the Niebroj-Dobosz et al. reference have been considered, in as much as they are relevant to the amended claims and the new rejection, but they are not persuasive.

Applicants' argue Niebroj-Dobosz et al. detects the presence of only 4 amino acids which are of interest to them and not 50 or more or 50% or more of the small molecules in the sample. Niebroj-Dobosz et al. meet the limitation of obtaining a small molecule profile of a sample from a subject suffering from a nervous system disorder as Applicants' define small molecules to be those of less than 2000 daltons. The amino acids detected by Niebroj-Dobosz et al. are less than 2000 daltons. Applicants' are correct that Niebroj-Dobosz et al. do not teach 50 or more or 50% or more of the small molecules in

the sample. However, Rashed et al. address this deficiency as they teach detecting all molecules in a blood sample to profile for metabolic diseases.

Applicants' further argue Niebroj-Dobosz et al. use HPLC methods which are selected to separate electrochemically active molecules which react with the fluorescent detectors and the detectors are specific for the amino acids of interest to them. Niebroj-Dobosz et al. meet the limitation of obtaining a small molecule profile of a sample from a subject suffering from a nervous system disorder. Niebroj-Dobosz et al. detect 4 specific amino acids which are less than 2000 daltons in a sample from a patient suffering from a nervous system disorder. It is irrelevant that the detection method is designed to be specific for amino acids in which they are interested. Additionally the method of HPLC can and is used as a way to determine and identify unknown compounds in a sample.

Applicants' argue Niebroj-Dobosz et al. do not teach using 2 or more detection methods. Applicants' are correct Niebroj-Dobosz et al. do not teach using 2 or more detection methods, however, Rashed et al. address this deficiency.

Finally, Applicants' argue Niebroj-Dobosz et al. do not teach identifying disease relevant small molecules by comparing a small molecule profile comprising information regarding two or more types of small molecules selected from the group consisting of sugars, fatty acids, amino acids, nucleotides, metabolites and products of catabolism as claimed in 77. Niebroj-Dobosz et al. do meet these limitations as Niebroj-Dobosz et al. teach detecting Glutamate, aspartate, glycine and GABA. These compounds are both amino acids and metabolites and catabolites. It is irrelevant Niebroj-Dobosz previously identified the amino acids in which they were interested in detecting. Niebroj-Dobosz compares the identified amino acids (which meet the limitation of small molecules) from a patient suffering from ALS to the same amino acids in a subject not suffering with ALS. The group of 4 amino acids constitutes a small molecule profile. and comparing the characteristics of the amino acids in the sample of the patient with ALS to one without ALS constitutes identifying disease relevant small molecules.

Conclusion

4. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Summary

5. No claims are allowable.

Correspondence

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Heather G. Calamita whose telephone number is 571.272.2876 and whose e-mail address is heather.calamita@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route. The examiner can normally be reached on Monday through Thursday, 7:00 AM to 5:30 PM.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at 571.272.0782.

Papers related to this application may be faxed to Group 1637 via the PTO Fax Center using the fax number 571.273.8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to 571.272.0547.

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hgc

JEFFREY FREDMAN
PRIMARY EXAMINER
8/31/07